HIV-Associated Progressive Multifocal Leukoencephalopathy: A Case Study

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ABSTRACT

Progressive multifocal leukoencephalopathy (PML) is a rare, life-threatening, infectious, lytic, demyelinating disease that results from reactivation of the virulent JC polyomavirus (JCV) "major opportunistic infection" in immunosuppressed individuals. We reported a case of a young girl who presented with new onset focal neurological defect, evaluated, and laboratory and radiological findings in the context of a clinical setting confirmed HIV-related-PML infection. However, remyelination does not occur, the patients may develop complications in the long term including cognitive impairment, sensory deficits, motor deficits, and disturbances in balance. We must increase our knowledge about HIV- related PML in any patient with reduced immunity and who presented with new onset neurological defect.

Keywords: *Progressive multifocal, leukoencephalopathy, JC virus, demyelinating disease.*

INTRODUCTION

Progressive multifocal leukoencephalopathy (PML) is a rare, life-threatening, infectious, lytic, demyelinating disease which affects glial cells in the white matter of the central nervous system.[1,2] Reactivation of the virulent JC polyomavirus (JCV) "major opportunistic infection" in immunosuppressed individuals with human immunodeficiency virus (HIV) infection, post solid organ and bone marrow transplant recipients, and malignancies causes PML disease.[3,4] The only known clinical manifestation results from the reactivation of dormant JC virus is PML. Although the cases associated with HIV account for about 85% of the cases that have been diagnosed with PML, the clinical entity of such presentation is to be suspected in patients who present with seizures, conscious level deterioration, and focal neurologic deficits.[5] Here, we reported a case of PML in an HIV-infected patient.

CASE ILLUSTRATION

A 13-year-old girl with normal perinatal and developmental history was admitted to the emergency department with the sub-acute onset of weakness of her right lower limb and deviation of mouth to the left side for one week. There was no history of seizure, headache, fever, disturbed conscious level, other cranial

nerves involvement, disequilibrium, sensory affection, or bladder disturbances. Her mother reported recurrent oral infection in the previous 6 weeks. She had a history of tonsillectomy at age of three years and left side hip surgery in her first year of life. The patient is right-handed without any history of medical importance. On examination, pulse was 75 beats/min, blood pressure was 110/70 mmHg and respiratory rate was 16/min. She was confused, limited verbal fluency, right lower motor facial nerve affection, right side hemiparesis (upper limb 4/5, and lower limb 3 /5), and extensor planter response bilaterally. The rest of the examination was normal. After admission, an urgent laboratory investigation was requested and showed normal blood pictures, electrolyte levels, blood gases, and biochemistry. Cerebrospinal fluid (CSF) analysis revealed normal biochemistry, cytology, culture, and sensitivity. CSF analysis for the virology panel was negative as well as negative for cryptococcal infection. CSF was also found negative for tubercular antigen by polymerase chain reaction. The patient started supportive treatment (intravenous fluid, vitamin), and brain imaging was requested. Magnetic resonance imaging (MRI) of the brain showed large confluent nonenhanced, infiltrative, ill-defined, subcortical, and cortical mass lesions, involving the left hemisphere, which crosses the midline to involve the right hemisphere via the splenium of the corpus callosum. Hemorrhage

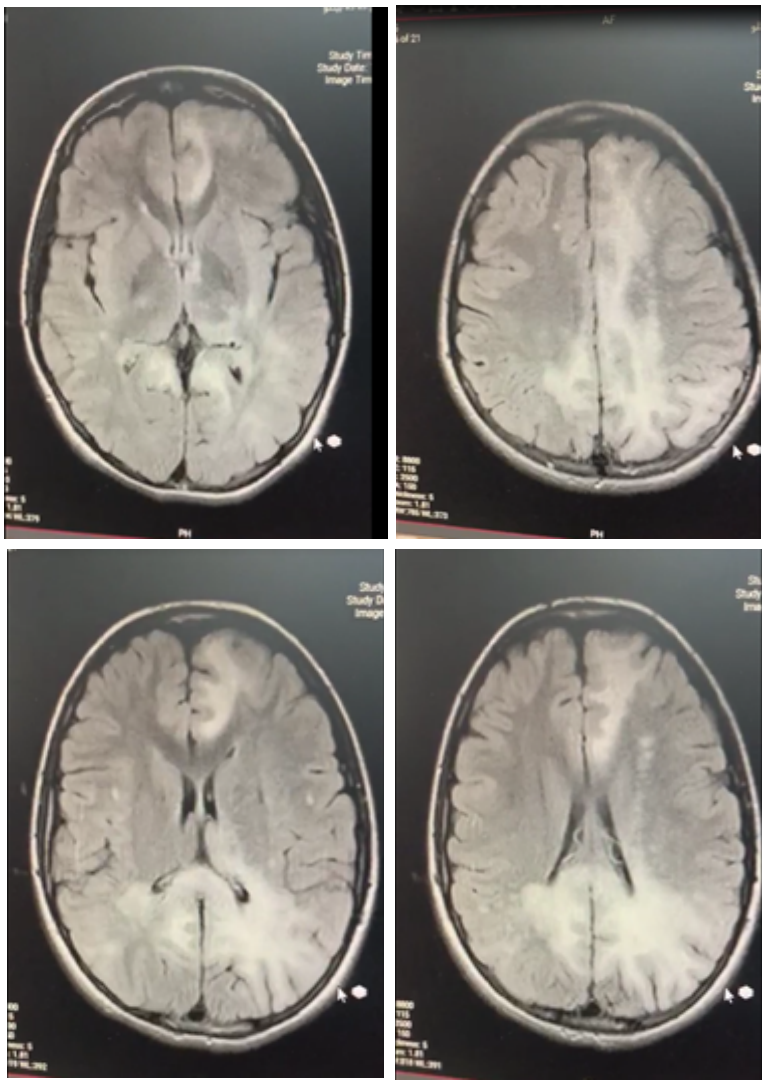

Figure 1. MRI of the patient's brain in the course of the disease shows large confluent non-enhanced, infiltrative, ill-defined, subcortical, and cortical mass lesions, involving the left hemisphere, which crosses the midline to involve the right hemisphere via the splenium of the corpus callosum.

or necrotic region is not detected. Infection of the CNS was suspected, and a blood sample for toxoplasmosis and virology screen was taken. ELISA for HIV-1 was positive. The absolute CD4 count was 120/μL. The possibility of PML was increased and confirmed with positive polymerase chain reaction (PCR) for JC virus in CSF. Given the above clinical features and investigations, the patient was diagnosed to have HIV-related PML. The patient started highly active antiretroviral therapy (HAART) with prophylaxis of opportunistic infections, but she died after 1 month.

DISCUSSION

The incidence of PML has increased significantly since the onset of the AIDS epidemic in 1981 and now HIV-associated cases account for up to 85% of all cases of PML. PML is a rare, life-threatening, demyelinating disease that affects the white matter of the central nervous system caused by the JC virus.[1] JC virus is a DNA virus of the polyomaviridae family that remains dormant in renal tubules and could be activated when the host developed any state of depressed immunity.[6] In a reduced immunity state, reactivation of the latent form of JC virus to cause active disease needs rearrangement of gene sequences in the virus DNA.[7] The natural course of the disease is determined primarily by the cellular immune response of the host particularly the cytotoxic T lymphocytes. In the case of reduced immunity, there was intense perivascular infiltration of immune cells, HIV antigens, and viral proteins resulting in severe, lytic demyelination. However, CSF has a major role in the clearance of the virus; we can depend on an elevated level of cytotoxic T lymphocytes in CSF samples of patients with suspicion of active PML.[8] PML should be considered in the differential diagnosis of any patient presented with a new onset neurological defect particularly when the CD4 count was less than 200. However, the most commonly involved sites include the subcortical white matter, periventricular areas, and cerebellar peduncles, the patients may manifest with variable presentation including cognitive decline, limb or gait ataxia, long tract affection, and aphasia.[7,8] Moreover, the presentation of PML could mimic different CNS infections clinically; toxoplasma encephalitis, primary CNS lymphoma (PCNL), HIV encephalopathy, and CMV encephalitis should be strongly considered in the differential diagnosis. Radiologically, PML is asymmetric, well-demarcated, and non-contrast-enhancing lesion without a mass effect, whereas both Toxoplasma and PCNL present as contrast-enhancing lesions.[8] Routine blood tests, infectious panel, and HIV PCR testing are indicated to identify the cause of the immunosuppressed state or any comorbid condition that led to the reactivation of the JC virus. The evaluation of abnormal neurological findings in immunosuppressed patients, such as those with AIDS, begins with Contrast-enhanced imaging with either CT or MRI to reveal the presence of inflammatory change and mass effect, and could help to differentiate the PML from other mimics.[9] The treatment for the complete cure of PML has not been found and is guided by the efforts made to boost the adaptive immune response of the patient.[10]

CONCLUSION

PML is a fatal, severe, progressive, multifocal, demyelinating disease. The main goal of current therapeutic approaches is directed at prolonging survival rates. However, remyelination does not occur, the patients may develop complications in the long term including cognitive impairment, sensory deficits, motor deficits, and disturbances in balance. We must increase our knowledge about HIV- related PML in any patient with reduced immunity and who presented with new onset neurological defect.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was conducted in concordance with declaration of Helsinki and the participant signed a written informed consent before being enrolled in the study. The institutional review board (IRB) approval was obtained from the ethical committee of Faculty of Medicine, Al-Azhar University, Cairo. The ethical code is “Near-Med._71 HIV- associated progressive multifocal leukoencephalopathy; a

case study._000071".

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTIONS

All authors participated in manuscript writing and editing. All authors have read and approved the manuscript.

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